2. DESCRIPTION OF CALCULATIONAL METHOD

2.1 Introduction

This section describes a way to obtain intake retention functions. These functions give the fraction of an intake of radioactive material expected to be present in a bioassay compartment at any time after an acute exposure or after onset of a continuous exposure. The intake is estimated from the quotient of the quantity of a radionuclide measured in a bioassay compartment by the intake retention fraction for that compartment. The intake can be compared to the NRC quarterly intake limit, the ICRP Publication 30 Annual Limit on Intake, or with other appropriate reference levels. This procedure for estimating intakes provides for a rapid assessment of the significance of measured results and thus provides a way to distinguish between exposures that require further investigation from exposures that do not. The model is based upon Reference Man models which are summarized in ICRP Publications 23 and 30 (ICRP74, ICRP79), but other metabolic models that fit the ICRP structure also can be used. The bioassay compartments may represent specific physiological entities such as the lungs or the gastrointestional tract, total body or excreta. Intake pathways which we consider here include inhalation and ingestion. We discuss the estimation of intakes and internal radiation doses and the frequency of monitoring required for detection. Our approach to obtaining intake retention functions can be implemented into any bioassay monitoring program that employs measurements on people or measurements of excreta.

Intake retention functions that are based upon Reference Man can be used to make a rapid assessment of the committed effective dose equivalent and the committed organ or tissue dose equivalent. The quotient of the estimated intake by the stochastic Annual Limit on Intake (ALI) value, which is given in ICRP Publication 30, when multiplied by 0.05 Sv (5 rem), gives the committed effective dose equivalent of an exposed worker.

One may also obtain organ or tissue dose equivalent by computing the product of the intake and the committed dose equivalent in target organs or tissues per intake of unit activity. A weighting factor representing the ratio of the risk arising from irradiation of the organ or tissue to the total risk when the whole body is irradiated uniformly may be multiplied by the committed organ or tissue dose equivalent. The sum of the weighted committed dose equivalents in target organs or tissues is the committed effective dose equivalent. The factors for dose equivalent per unit activity intake (Sv per Bq) appear in supplements to ICRP Publication 30. Age and gender averaged

weighting factors appear in ICRP Publication 26 (ICRP77), but under certain circumstances they may be modified to reflect competing causes of death or reflect the gender of the exposed person. Thus, a more direct estimate of weighted committed, or committed organ and tissue, dose equivalent may be made from the estimate of intake and the Sv per Bq factors.

Nuclear facilities are designed so that combined exposures to people from external and internal radiation sources are maintained below the ICRP and the proposed NRC committed dose limits (See ICRP77 or NRC84). It is important that internal dose assessment procedures, as well as investigation, action, and recording reference levels be established with respect to these committed dose limits. A quantity derived from these committed limits is the Annual Limit on Intake given by ICRP. To assure that significant internal radiation exposures are detected, properly investigated, and recorded, all internal radiation dose assessment procedures should be designed to translate measurements into estimated intakes. Otherwise, significant doses, for example the dose to the lungs, may be neglected if only the systemic burden is estimated from excretion bioassay measurements. Because of the direct relationship between intake and committed dose, the use of intake provides a way to combine external and internal doses. Thus, the total committed organ dose or the committed effective dose equivalent to the whole body can be estimated for exposures received by workers during each year of practice.

The detection of an intake that is significant with respect to the ALI may require monitoring of both the working environment and the worker. Neither bioassay nor air sampling are mutually exclusive; both may be required for an accurate assessment of internal radiation exposures (Sk85). When bioassay procedures do not have the required sensitivity and accuracy, then breathing zone air-sampling should be used to estimate intakes by workers having a potential for significant exposures. Accurate assessments of exposures often require a proper balance between monitoring the environment and monitoring workers. Additionally, information on the physical and biochemical characteristics of radionuclides, which can be obtained from monitoring the working environment, may be used with Reference Man metabolic models to generate intake retention functions that are needed for the estimation of intakes from bioassay data.

Intake retention functions, which give the fractions of an intake expected in various in vivo and in vitro bioassay compartments at any time, provide necessary information for a rapid and efficient determination of the significance of bioassay results. In addition, intake retention functions can be used in the design and operation of a bioassay program. For example, numerical values obtained for intake retention functions can be used to identify those bioassay procedures that have sufficient sensitivity. They also can be used to calculate derived investigation levels. Following accidents, values for intake retention functions can be used to identify special bioassay procedures that confirm and improve estimates of intake.

In the following, we discuss applications of intake retention functions, including some of their limitations. The text includes derivations of these functions, derivations which are made via the application of a single catenary kinetics equation to a multicompartmental model. These derivations are based upon models that describe the transport and retention of elements from intake to excretion. The recursive nature of the catenary kinetics equation facili-

tates programming on calculators or computers. Details related to the derivation of various types of intake retention functions and details related to fitting of repetitive bioassay measurements are also provided.

Sections 2.2 through 2.5 provide a detailed description of the calculational procedures used to derive the tabulations of intake retention fractions for use with *in vivo* and *in vitro* measurements. The main points of the description are:

1. the tables, which are derived from the equation given in Section 2.5.1, give the fraction of intake retained, the fraction excreted in 24 hours, and the fraction accumulated in excreta as a function of time post intake;

2. intakes can be estimated by dividing the measured value, for lung, thyroid, whole-body, urine or fecal activity, by the IRF value which is associated with the compartment of interest;

3. derived investigation levels can be set below which no action is required, and above which further measurement to estimate committed effective dose equivalent should be made; and

4. it is unrealistic to assume that individual results will fit model results in most exposure cases. The magnitude of the uncertainity is indicated in Appendix A, Example of Use Based on Experiences.

If you require a detailed description of the calculational method, please read Sections 2.2 to 2.5, otherwise, advance to Section 3, Retention and Excretion Fraction Tables.

2.2 Terminology Needed for Interpretation of Bioassay Measurements

There are various quantities or terms used by health physicists for bioassay and internal dose assessment and various retention functions have been associated with these quantities. The definitions of these quantities are important in order to understand the mathematics used in the derivation. Terms or quantities include *intake*, *uptake*, *deposition*, and *content*:

intake = quantity of a radioelement taken into the body by inhalation, ingestion, or wound,

uptake = quantity of a radioelement taken up by the systemic circulation, e.g., by injection into the blood, by absorption from compartments in the respiratory or GI tracts, or by absorption near the site of a wound,

deposition = quantity of a radioelement deposited, e.g., in the respiratory tract following an acute inhalation intake or in the stomach following an ingestion intake,

content = quantity of a radioelement present in some bioassay compartment of the model, which may be an organ, a group of tissues, the whole body, or an excretion compartment.

fundamental rate constant = the instantaneous fractional rate of removal of the content of a compartment by biological processes only.

Each type of retention function applies to the content of a particular compartment, relative to the referenced quantity. Thus, each type of function yields the fraction of an intake, uptake, or a deposition expected in the compartment at some time t, post an intake, uptake, or deposition, respectively. In general, upper case letters are used as symbols in equations in order to represent quantities for stable elements while lower case letters are used to represent quantities for radionuclides. Subscripts are used to identify compartments.

Consider an acute inhalation intake of radioactive aerosols in which 63% of the inhaled activity is expected to deposit in the lungs. The initial fraction of the intake expected to be deposited in the lungs, which is given by the intake retention function for the lungs for t equal 0, is 0.63, while the initial fraction of the deposition expected to be present in the lungs, which is given by the deposition retention function for the lungs for t equal 0, is 1.0. The uptake retention function gives the fraction of an acute uptake expected in some compartment at some time after an uptake. The values of the uptake retention functions for the systemic whole body and the extracellular fluid must equal 1.0 for t equal 0. The values of the uptake retention functions for peripheral tissues and organs must equal 0 for t equal 0.

Another important term is fundamental rate constant. Removal can involve excretion from the body or simply return to extracellular fluid. A fundamental rate constant can be associated with any organ or tissue. These fundamental rate constants may be difficult to determine because a portion of the deposition once removed from an organ may be returned to that organ at some later time. Thus, a measured rate of loss from the organ would appear to be slower than the fundamental rate of loss because small amounts of material may be recycled back to the organ.

The uptake retention function is a mathematical construct or empirical function that may have several exponential terms. Under certain conditions some of these terms may be associated with physiologically identifiable compartments. One term in the construct may represent the central compartment if there is no significant recycling. The central compartment may be vaguely defined as the compartment which includes blood and extracellular fluid, i.e. material in this compartment is free-moving. The remaining terms in the mathematical construct may be associated with peripheral organs, such as bone or thyroid. Material in these compartments includes that contained in cells plus that attached to organ surfaces. Again, this physiologic association is purposely vague and applies only if there is no significant recycling.

If the metabolic process, which describes the removal of a radioelement from a compartment, is described by linear first-order kinetics, then the deposition retention function is given by a single exponential term, with coefficient of unity. This simple deposition retention function gives the fraction of deposition expected at some later time. This type of deposition retention function is used for the stomach for intake via ingestion as well as some compartments within the respiratory tract.

If the retention of a systemic organ or tissue is simple, then the organ's deposition retention function is given by a single exponential term, with a coefficient of unity. The function represents the fraction of a single deposition expected at some time after deposition, neglecting any recycling of

the element. However, because of recycling, such deposition retention functions would not describe the actual content of organs or tissues.

If there is no direct excretion from an organ, the fundamental biological rate constant, which is a term in the exponent of an organ deposition retention function, describes the transfer of a stable element to the central compartment. The deposition retention function of a single organ may be given by a single exponential term, but on the other hand, the uptake retention function for that same organ, will often be given by a sum of exponential terms with constant coefficients. The algebraic sum of these coefficients must equal 0 at t equal 0. A number of peripheral organ and tissue compartments could each have a simple deposition retention function described by a single exponential term containing a characteristic fundamental rate constant. The value of this rate constant would characterize total biological removal to direct excretion or the central compartment.

If significant recycling of the stable element occurs, then the uptake retention functions for each peripheral compartment and for the central compartment would contain the same number of exponential terms. However, rate constants in these exponential terms would not equal the fundamental rate constants. In the case of recycling, the uptake retention function of each compartment and the uptake retention function of the systemic whole body would have the same exponential terms but different coefficients. If significant recycling does occur, the rate constants in the uptake retention function for the systemic whole body do not describe the actual retention of a deposition within a specific compartment. These rate constants are effective rate constants, which account for recycling of a contaminant between the central and peripheral compartments. In such a case, no single exponential term can in reality be associated with a particular structured compartment (Sk80).

If there is no significant recycling, the rate constants in the uptake retention functions equal the fundamental rate constants. In such a case, the stable element uptake retention function for the central compartment would be given by a single exponential term. This central compartment term would contain the fundamental rate constant that describes removal by all pathways. In the case of no significant recycling, the uptake retention function for a stable element for each peripheral organ compartment would contain two exponential terms, one with the fundamental total removal rate constant for the central compartment and one with the total biological removal rate constant for the organ. In such a case, the individual exponential terms in the uptake retention function for the systemic whole body could be associated with specific tissues or organs.

The description of the distribution and retention of elements in ICRP Publication 30 (ICRP79) has descriptive simplifications that relate to recycling. Because individual exponential terms of most retention functions cannot be associated with specific organs, care must be exercised in using the ICRP Publication 30 description for the development of bioassay models which are needed to make an initial assessment of the significance of bioassay data. Additionally, we do not include the ICRP so called "transfer compartment" in the derivation of our intake retention function. The ICRP adds this transfer compartment for mathematical convenience (ICRP79) while in fact the retention of any transfer compartment must already be included in the systemic whole body, empirical, uptake retention function.

2.3 Limitations Associated With The Use Of Metabolic Models

Many assumptions are required to translate bioassay data into estimates of intakes and internal radiation doses. Such assumptions may include parameter values for the fraction of systemic excretion passing into the bioassay excretion compartment as well as assumptions regarding uptake following deposition of the radionuclide in the respiratory tract. Because of the physical, chemical, and biological complexities that affect the distribution of a radionuclide within the body, neither the annual nor committed effective dose equivalent can be obtained from the whole body retention function without making many assumptions. Assumptions that may have order of magnitude impact apply to single excreta bioassay measurements. This uncertainty can be reduced by collecting several samples in sequence. Although frequent and careful excreta measurements can be used to obtain the worker's excretion function applicable to the time over which measurements are made, many assumptions including the physical and biochemical characteristics of the inhaled aerosol, the uptake fraction, and the systemic excretion fraction will be required for the estimation of intakes and internal radiation doses.

To estimate the intake and corresponding internal radiation doses, a practical alternative is to use information on the known physical and biochemical characteristics of inhaled radionuclides, and apply these assumptions to the applicable metabolic model for Reference Man. This is the basis for the practical use of intake retention functions that are based on Reference Man or other appropriate models.

2.4 Intake Retention Functions and Their Applications

Intake retention functions can be used in the design and conduct of bioassay programs. They can be used to generate tabular values for stable or radioactive element intake retention fractions (IRFs) as well as derived investigation levels. Such derived investigation levels can provide the operational health physicist information on procedures which have the required sensitivity and accuracy for the minimum amount that can be detected by a given bioassay procedure.

When large accidental exposures occur, attempts should be made to estimate the actual retention and dose distribution in the exposed worker rather than rely on Reference Man models. In such cases, the uncertainties associated with using the individual's own metabolic parameters in the estimation of the committed doses should be evaluated carefully.

When a number of bioassay measurements are used to evaluate an incident, the intake retention function, which is derived from Reference Man metabolic models, can be used as a fitting function. The amount of the intake is then estimated as that which gives the best fit of individual measurements to their respective expectation values that are obtained from the product of the estimated intake and values derived from the intake retention fitting function. This procedure certainly is justified in most cases where limited and poor bioassay data are available. If more extensive and accurate bioassay data are available from accidental exposure cases, then the residuals obtained from the difference between measurements and the expectation values should be examined for any apparent structure and discrepancy associated with the use of an intake retention function derived from Reference Man models. If large discre-

pancies are noted, then attempts should be made to improve the assumptions and parameter values used to derive the intake retention function used in the fit.

Committee 4 of the ICRP has published two reports relating to the evaluation of radiation doses from bioassay data, Publication 10 (ICRP68) and Publication 10A (ICRP71). These publications are limited to the evaluation of uptakes as opposed to intakes. Because of the delay in uptake from compartments in the respiratory and GI tracts to the systemic organs, models that incorporate this delay in uptake are needed. Specifically, what are needed are intake retention functions, which give the fractions of an intake expected in bioassay compartments at various times after an intake.

2.5 Catenary Pathways from Intake to Excretion

The metabolism of elements is described here by linear first order kinetics which can be depicted as one way transfers between compartments; transfers that begin with some intake compartment and end with some excretion compartment as depicted in Figure 2.1. The term catenary refers to a one-way chain in which material is transfered from one compartment to another. The metabolism of all elements can be described in this way. Because the metabolism can be described in terms of these simple one way transfers, a recursive catenary kinetics equation can be used to obtain the expected content of all *in vivo* and *in vitro* bioassay compartments. Even though the metabolism is described by these one-way tranfers, the intake retention functions derived from this model account for recycling within the systemic whole body provided that an appropriate whole-body systemic uptake-retention function is used in the derivation. An excretion compartment is simply treated as the last compartment in each chain. Removal of a radioelement from an excretion compartment is described entirely by its radioactive decay constant, while total removal from an *in vivo* compartment is described by the sum of the decay constant and all applicable biological removal rate constants. It is recognized that this model and description of the metabolism is a gross oversimplification of the actual metabolism.

Provided that appropriate values are chosen and lacking more specific details, the catenary model can provide reasonable values for the intake retention fractions. On the other hand, care must be exercised in the interpretation of the short term kinetics, especially during the first few days following accidental intakes.

Chains of compartments can be determined for inhalation intakes, ingestion intakes, instantaneous uptake, or exponential uptake, for example from a wound. If several chains lead to a particular compartment of interest, the total retention function for that compartment is obtained by summing the contributions from all chains. If a system of organs and tissues, such as the systemic whole body, is modeled as if it were comprised of a number of independent catenary compartments, the total retention function is obtained from the sum of retention functions for the individual compartments.

There are a number of chains for each type of intake and each chain begins with an intake compartment and ends with an excretion compartment. Chains involving inhalation intakes, with depositions into various regions of the respiratory tract, are shown on the upper left, and pathways involving ingestion intakes are shown on the right in Figure 2.1.

Inhalation involves eight compartments of deposition in the respiratory tract, each of which initiates a separate catenary system. Ingestion begins with one compartment of deposition, the stomach.

Arrows leaving a compartment show the specific removal pathways, which are characterized by specific translocation rate constants for particular pathways. In addition to biological removal, radioelements are removed from each catenary compartment by radioactive decay, which is characterized by the decay constant for the radioelement.

Compartments associated with the respiratory tract are shown on the upper left hand side of Figure 2.1. The arrows designated by $D_{NP}I$, $D_{TB}I$, and D_PI represent depositions in the three regions of the respiratory tract. These arrows lead into the nasal passage region (NP), tracheobronchi region (TB), and pulmonary region (P) of the respiratory tract. The symbol I represents the intake and D_{NP}, D_{TB}, and D_P represent the fractional depositions. The deposition fractions for an inhalation intake of 1 micrometer AMAD aerosols are 0.3, 0.08, and 0.25 for the NP, TB, and P regions, respectively.

Compartments a, c, and e shown on the left-hand side of the respiratory tract schematic are cleared directly to the systemic circulation. Compartment h represents clearance to the lymph nodes, which are comprised of two compartments i and j. Compartment i clears to the systemic circulation and compartment j is a sink. The only removal from compartment j is by radioactive decay. Compartments b, d, f, and g are shown on the right hand side of the schematic and are cleared to the stomach.

The fraction of a deposition cleared by a particular pathway and the associated clearance half-time are designated for three chemical compound classifications: days (D), weeks (W), and years (Y), which are representative of the clearance half-times from compartments e. g, and h in the pulmonary lungs. These clearance half-times are 0.5, 50, and 500 days for Class D, W, and Y compounds, respectively. However, there is no clearance for compartment g for Class D compounds since there is no deposition in it.

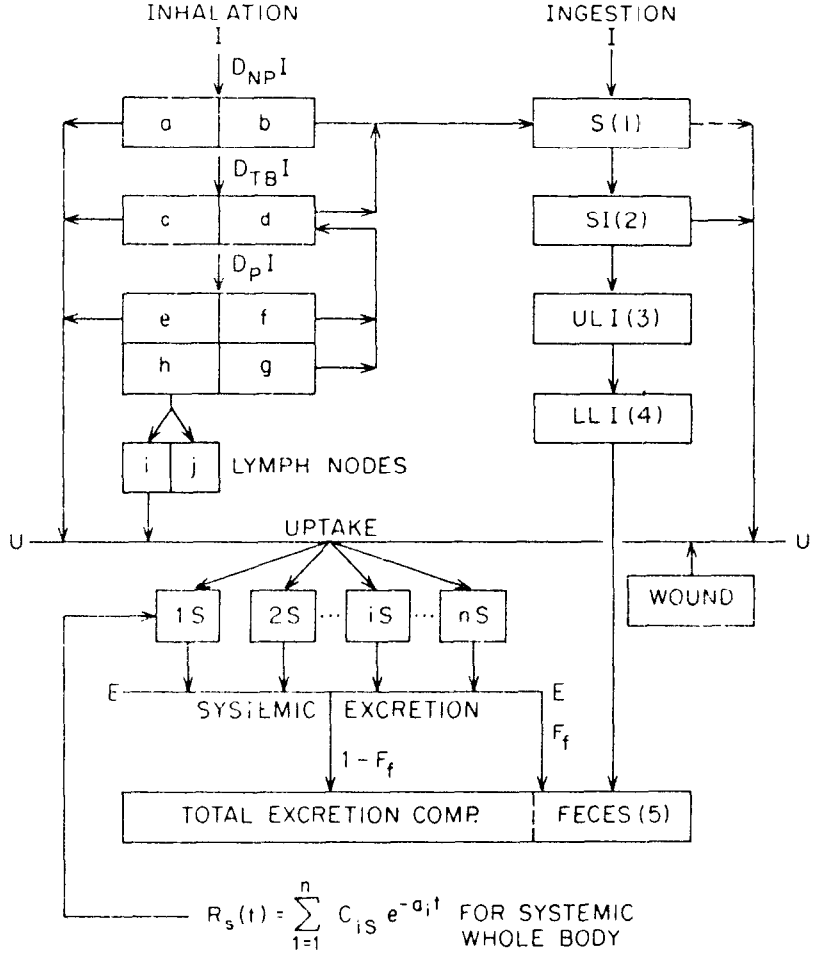

FIGURE 2.1 Catenary pathways from intake to excretion. Respiratory tract compartments are a through j. Gastrointestinal tract compartments are 1 - 4. $R_S(t)$ defines the stable element uptake retention function for the systemic whole body which is expressed by a sum of exponential terms (i = 1 to n) with constant coefficients.

Shown on the right-hand side of Figure 2.1 are the four segments of the gastrointestinal tract. An ingestion intake is first deposited in the stomach. The intake is translocated from one segment of the gastrointestinal tract to another and then finally to the feces, which are designated here as compartment 5. The feces are considered part of the total excretion compartment. In ICRP Publication 30, instantaneous uniform mixing and linear first-order kinetics are assumed to apply to each segment of the tract. These assumptions result in an overestimate of the early fecal excretion. The mean residence time in each segment of the tract are 1 hour for the stomach, 4 hours for the small intestine, 13 hours for the upper large intestine, and 24 hours for the lower large intestine. Partial absorption of a radioelement into the blood is assumed to occur only in the small intestine. If the radioelement is completely absorbed, absorption is considered to occur from the stomach, and this pathway is shown by a broken arrow to the upper right of Figure 2.1. The translocation rate constant that is associated with this pathway is simply set equal to 24 day^{-1}, which is that associated with the removal of the contents from the stomach. The inverse of the mean residence time for the contents of each segment gives the translocation rate constant for both the contents and contained radionuclides.

Absorption into the systemic circulation is shown to lead to a horizontal line designated by U, which represents uptake. Absorption into the systemic circulation itself is identified by the symbol S. All pathways combine at U and then divide into n compartments. These compartments are designated by the n exponential terms in the whole-body systemic uptake retention function $R_S(t)$ shown at the bottom of Figure 2.1.

The second translocation rate constant, which describes transfer from a compartment that feeds a systemic compartment via uptake into the systemic circulation, is obtained by multiplying the first translocation rate constant from the feed compartment to the systemic circulation by the coefficient C_{iS} of the exponential term in $R_S(t)$ that pertains to the pseudo catenary compartment of interest. For example, consider an ingestion intake where $f_1 = 1$ so that the translocation rate constant $k_{1,s}$ of 24 day^{-1} describes transfer from the stomach to the systemic circulation. To obtain the rate constant $k_{1,iS}$, which describes transfer from the stomach to the iS compartment, the rate constant $k_{1,s}$ is multiplied by the coefficient C_{iS} for the psuedo catenary compartment of interest.

Each i^{th} exponential term in $R_S(t)$ is treated as a deposition retention function of a pseudo catenary compartment, and each compartment is modeled to be cleared directly to systemic excretion E at an instantaneous fractional rate given by the effective rate constant a_i of the i^{th} exponential term. The effective fraction of an uptake U that passes into the i^{th} pseudo catenary compartment of the systemic whole body, as noted above, is given by the coefficient C_{iS} of the exponential term in $R_S(t)$.

Because the intake retention function $R_S(t)$ embodies, in principle, all of the dynamic processes that describe the metabolism of stable elements in the systemic whole body, including the recycling of elements, the intake function $I_S(t)$ which is derived from the function $R_S(t)$ also embodies all these metabolic processes plus the metabolic processes that occur in all of the compartments that feed the systemic circulation. It is fortunate that each exponential term of the uptake retention function for the systemic whole body

can be treated as a deposition retention function for a pseudo catenary compartment. It greatly simplifies the derivation of intake retention functions from the general catenary kinetics equation shown as equation 2.5.1 below.

Atoms of a radioelement that leave one of the pseudo catenary compartments of the systemic whole body are shown to go directly to systemic excretion, which is designated here by a horizontal line identified by E in Figure 2.1. The rate constant that describes the fractional rate of excretion from each iS compartment is the eigenvalue rate constant a_i in the exponential $\exp(-a_i t)$ of the uptake retention function $R_S(t)$. The i^{th} exponential term of $R_S(t)$ thus represents the deposition retention function for the iS compartment, and loss from this compartment is shown to go directly to excretion. Because parameter values in $R_S(t)$ are effective values that incorporate recycling, it can be shown that this interpretation is mathematically correct.

The line E is necessary for designating the fraction of excretion that leaves the systemic whole body via the fecal excretion pathway, and by all other pathways. The fraction f_f of systemic excretion via the fecal pathway is shown to enter feces directly. The primary pathway is probably that involving biliary excretion, which passes into the duodenum or first part of the small intestine. The systemic fecal excretion pathway is shown here to bypass the GI tract. Thus, the fraction f_f of systemic fecal excretion should be considered an effective value.

Although this model simplifies the mathematics, it is not realistic. Because of the lack of data for the systemic fecal excretion pathway, this simplifying assumption seems reasonable for developing bioassay models.

All systemic excretion, as well as direct fecal excretion, is shown in Figure 2.1 to end up in the compartment that is designated as the total excretion compartment. This compartment is treated as any other catenary compartment; it is the last compartment of all catenary systems. The only removal process from this compartment is radioactive decay. Thus, the total removal rate constant k_j that describes removal from this compartment is set equal to the decay constant λ for a radioelement, or zero for a stable element.

Intake retention functions for acute inhalation can be obtained for specific organs, organ systems, and excretion by summing the functions for the appropriate compartments. This includes: (1) the nasal passages, compartments a and b; (2) the lungs, compartments c through j; (3) the GI tract, compartments 1 through 4; (4) the systemic whole body, compartments 1S through nS; (5) a specific systemic organ x, compartments 1x through nx corresponding to the exponential terms in the stable uptake retention function $R_x(t)$ for the organ x; (6) the accumulated total systemic excretion, compartment E; (7) the accumulated total fecal excretion, compartment 5; (8) the accumulated urinary excretion, which is obtained from the product of f_u times the intake retention function for compartment E if f_u is constant; and (9) the total body, which is the sum of (1) through (4) above. In the same way as above, intake retention functions can be obtained for ingestion intakes, instantaneous uptakes, or delayed uptakes through a wound.

To apply a general catenary kinetics equation, one must identify the appropriate chains of compartments, specify the translocation and total removal rate constants within each chain, and specify the decay constant for the radio-

element. Numerical values for the fraction of an intake expected in a compartment are easily obtained because the same recursive kinetics equation is used for each chain that leads to the compartment of interest.

2.5.1 Radioelement Intake Retention Function $i_n(t)$ for n^{th} Catenary Compartment

The concise catenary kinetics equation shown here as equation 2.5.1 can be applied to all of those catenary pathways that lead to an n^{th} compartment of interest to obtain the radioelement intake retention function $i_n(t)$ for that compartment:

$$i_n(t) = \sum_C F_C \left[\prod_{p=1}^{n-1} k_{p,p+1} \left[\sum_{j=1}^{n} \frac{e^{-k_j t}}{\prod_{\substack{p=1 \\ p=j}}^{n} (k_p - k_j)} \right] \right] \qquad 2.5.1$$

where:

$i_n(t)$ = fraction of a single acute intake of radioelement expected at time t in n^{th} compartment,

C = one of the chains that leads to the n^{th} catenary compartment of interest,

F_C = fraction of intake deposited into the first compartment of chain C,

$k_{p,p+1}$ = rate constant that describes transfer of element from p^{th} to $(p+1)^{th}$ compartment,

k_j = total rate constant that describes total removal of the radioelement from the j^{th} compartment, and given by the sum of the total biological removal rate constant K_j and the decay constant λ of the radionuclide, and

k_p = total rate constant describing removal from p^{th} compartment.

The subscript n on $i_n(t)$ is a general numerical index for the compartment of interest. For a given catenary pathway that leads to an n^{th} compartment of interest, n could have one value. For another pathway, the particular compartment of interest could then be symbolized by another value of n or perhaps the same value. For example, consider the intake retention function $i_d(t)$ for compartment d in the TB region of the respiratory tract. Three catenary systems contribute to the fraction of an inhalation intake that is present in compartment d. These are direct deposition for which n=1, translocation to compartment d from compartment f for which n=2, and translocation to compartment d from compartment g for which n=2.

In the case where two different compartments have the same value for transfer rate constant, $k_p = k_j$, one can make k_p a little different from k_j, and thus be able to use equation 2.5.1. The error is the same order of magnitude of the

difference assumed between k_p and k_j. Assuming a small difference, <10 E-4%, yields accurate results for i_n (Bi86).

The ICRP Publication 30 respiratory tract model provides the parameter values needed for the application of equation 2.5.1. The parameter values generally depend on the particle size distribution and the compound classification of the inhaled aerosol. Particles containing a radioelement and soluble materials that are translocated from compartments f and g to compartment d are assumed to instantaneously mix with the contents of d, which is cleared by translocation to the stomach. The translocation to the stomach, S(1), from d is described by a translocation rate constant $k_{d,1}$, which can be obtained from the clearance half-time of 0.2 days given in ICRP Publication 30 for all compound classes.

Equation 2.5.1 is summed over three separate chains C in order to obtain the intake retention function $i_d(t)$ for compartment d in the TB region of the lungs. The radioelement intake retention function $i_L(t)$ for the lungs is obtained by repeating this procedure for the other lung compartments c, e, f, g, h, i, and j, all of which may or may not be applicable for each chemical compound classification. For example, for the highly transportable compound Class D, the clearance pathways designated by f and g are not used.

2.5.2 Inhalation Intake Retention Functions for Lungs

Figure 2.2 shows values for the stable element acute intake retention functions $I_L(t)$ for the lungs for Class D, Class W, and Class Y compounds and for the inhalation of 1 micrometer AMAD aerosols by Reference Man. The curves are for an intake at time zero. The plots show that in vivo lung counting can be a practical bioassay procedure for the highly transportable Class D compounds only if measurements are made soon after an exposure incident. Because of the large and early absorption into the systemic circulation, in vivo whole-body counting may be used as an alternative procedure for Class D compounds. Lung counting is applicable to Class Y compounds and practical for Class W compounds for tens of days post intake. For Class Y compounds, compartment j is a sink that will ultimately contain 0.00375 of an inhalation intake of a stable element contained in 1 micrometer AMAD aerosols. Thus, the limiting value for $I_L(t)$ is 0.00375 for stable Class Y compounds. Lung counting would not be a practical bioassay procedure for the inhalation of non-respirable particles having sizes above about 20 micrometers. However, GI tract counting and/or fecal analysis could then be practical. In accidental intake cases, these curves and a series of lung measurements can be compared in order to estimate the compound classes and intakes.

2.5.2.1 Inhalation Intake Retention Functions for GI Tract and Accumulated Feces

Figure 2.3 shows values for the acute intake retention functions for the GI tract contents and for the accumulated feces compartment for Class D, Class W, and Class Y compounds. The curves are for an inhalation of 1 micrometer AMAD aerosols at a time of zero. The functions were evaluated for the case where the fraction f_1 absorbed into the blood from the small intestine and the fraction f_f of systemic excretion via the fecal pathway are both zero.

The plots show that the GI tract segments can contain up to 40% of an inhalation intake of 1 micrometer AMAD aerosols, during the first weeks post intake.

This fact should be taken into consideration for the proper interpretation of a lung count or a whole body count when the GI tract contents contribute significantly to the response of the detector.

The plots show that the accumulated fecal compartment will contain up to about 60% of an element contained in an inhalation intake of 1 micrometer AMAD aerosols. In serious exposure cases, it is recommended that all of the fecal excretion over the first five or six days be collected and analyzed. This will make the measurements less sensitive to the model assumptions and will give a better estimate of the respiratory tract deposition cleared to the fecal excretion pathway.

2.5.2.2 Inhalation Intake Retention Functions for Systemic Whole Body and Urinary Excretion for Stable Cobalt

Figure 2.4 shows the expected systemic retention and urinary excretion after a single inhalation intake of stable cobalt. The plots apply to Class W compounds and 1 micrometer AMAD aerosols. The ICRP Publication 30 respiratory and GI tract models were used to obtain the values for these intake retention functions. The systemic whole-body uptake retention function $R_S(t)$ given in ICRP Publication 30 was used according to the procedure outlined in Figure 2.1. The value of 0.05 was used for the fraction f_1 of stable cobalt absorbed from the small intestine into the blood. The value of 0.8 was used for the fraction f_u of systemic excretion via the urinary pathway. We note that 0.8 for f_u was used based upon a better fit to the reported urine data used to obtain the ICRP Publication 30 model for stable cobalt.

Values that are plotted for stable cobalt include: (1) the systemic whole-body intake retention function, which gives the fraction of a single intake that is expected to be present in the systemic whole-body at time t post the intake; (2) the accumulated urine intake retention function, which gives the fraction of intake expected to be present at time t in accumulated urine; (3) the 1 day incremental urine intake retention function, which gives the fraction expected to be present at time t in an incremental sample of urine that is collected from day t-1 to t post intake; and (4) the instantaneous urine excretion rate function, which gives the instantaneous fraction of the intake that is expected to be excreted per day in the urine at time t post intake. When *in vivo* or *in vitro* bioassay measurements are made at time t, the intake is estimated by dividing the results corrected for decay by the value of the applicable stable element retention or excretion functions, respectivity, evaluated at t.

It is not correct to consider an early 24 hour sample as an instantaneous daily rate of excretion. As can be seen from Figure 2.4, the incremental function for cobalt exceeds the instantaneous function at early times by a factor of 2. Only after about 10 days do values for these two functions come close to one another. Thus, a procedure that is used for evaluating spot urine measurements as instantaneous rates of excretion can give high estimates of the intake and associated dose equivalent.

The log-log plots of the urinary excretion of cobalt, following a single acute inhalation intake of 1 micrometer AMAD, Class W aerosols, approximate straight lines. One might conclude that the underlying metabolism, considering the normal variance that is expected in bioassay measurements, is best described by a power function in time. However, such a conclusion would be wrong because these plots are based upon linear first order kinetics that yield a sum of exponential terms with both positive and negative constant coefficients.

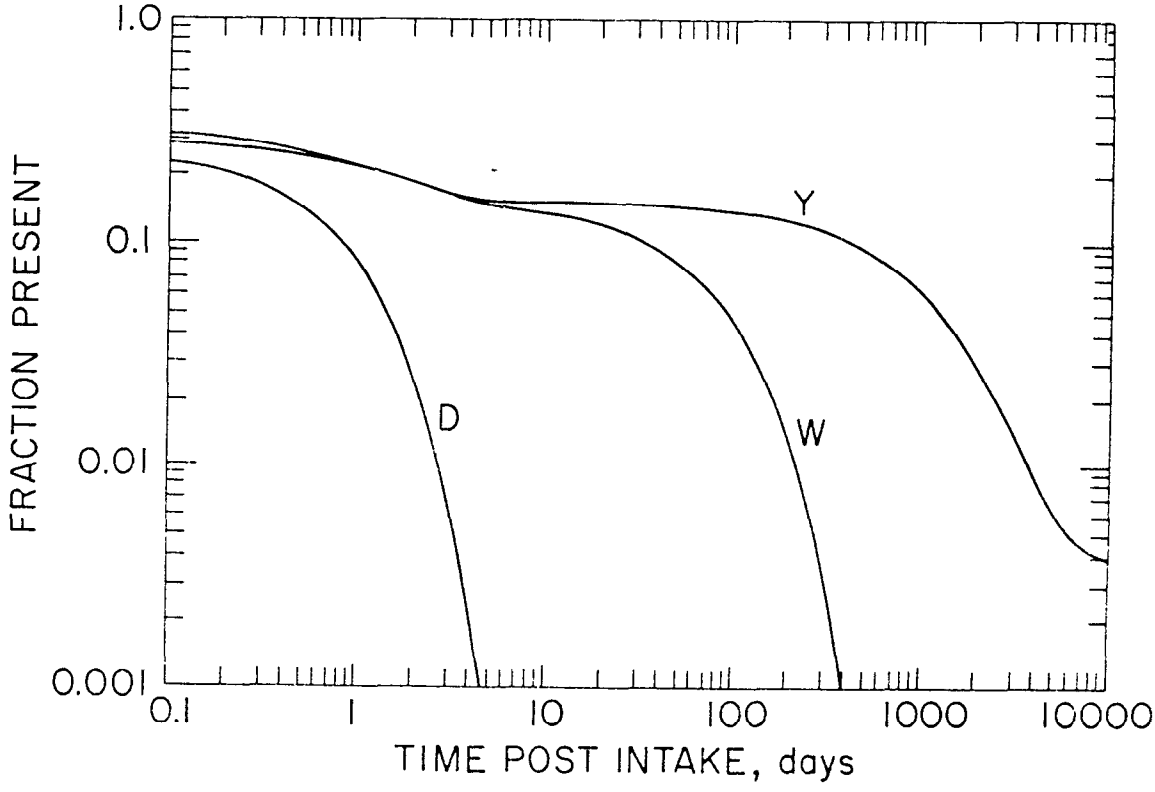

FIGURE 2.2 Inhalation intake retention functions for lungs for 1 micron AMAD aerosols of stable Class D, W, or Y compounds.

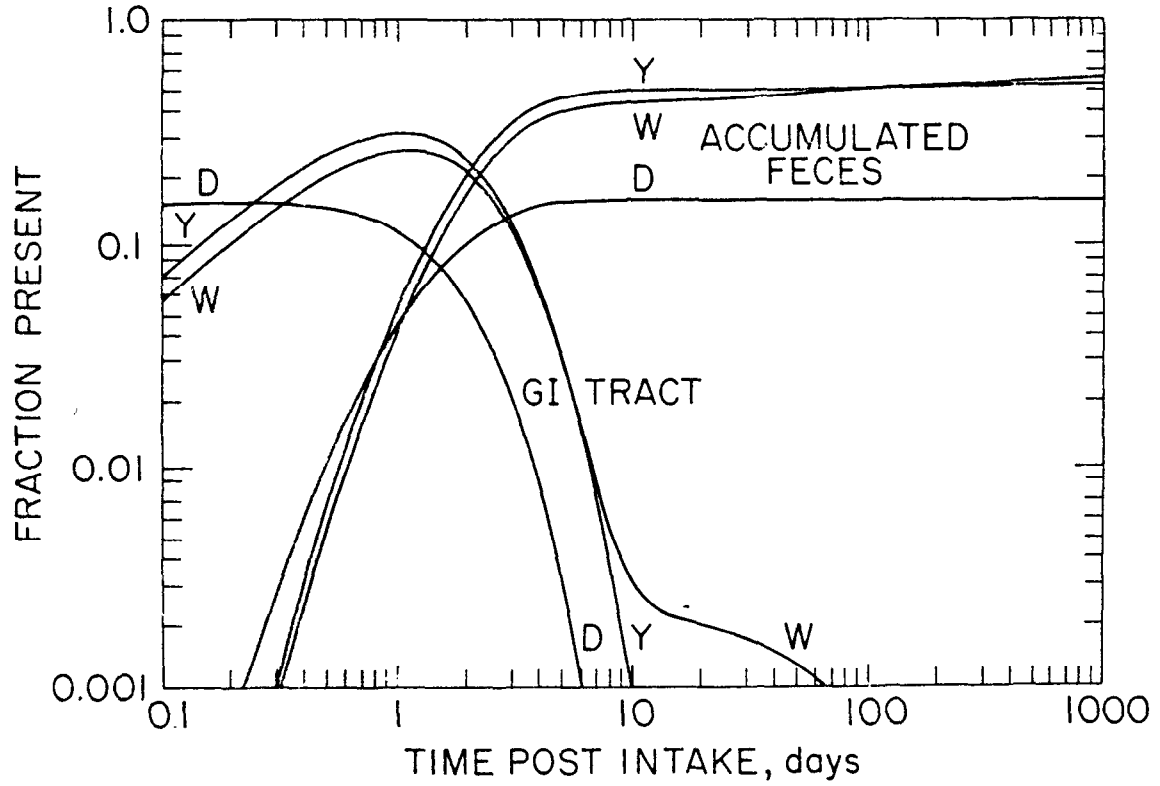

FIGURE 2.3 Inhalation intake retention functions for GI tract and accumulated feces for 1 micron AMAD aerosols of stable Class D, W, or Y compounds for which f_1 and f_f equal zero.

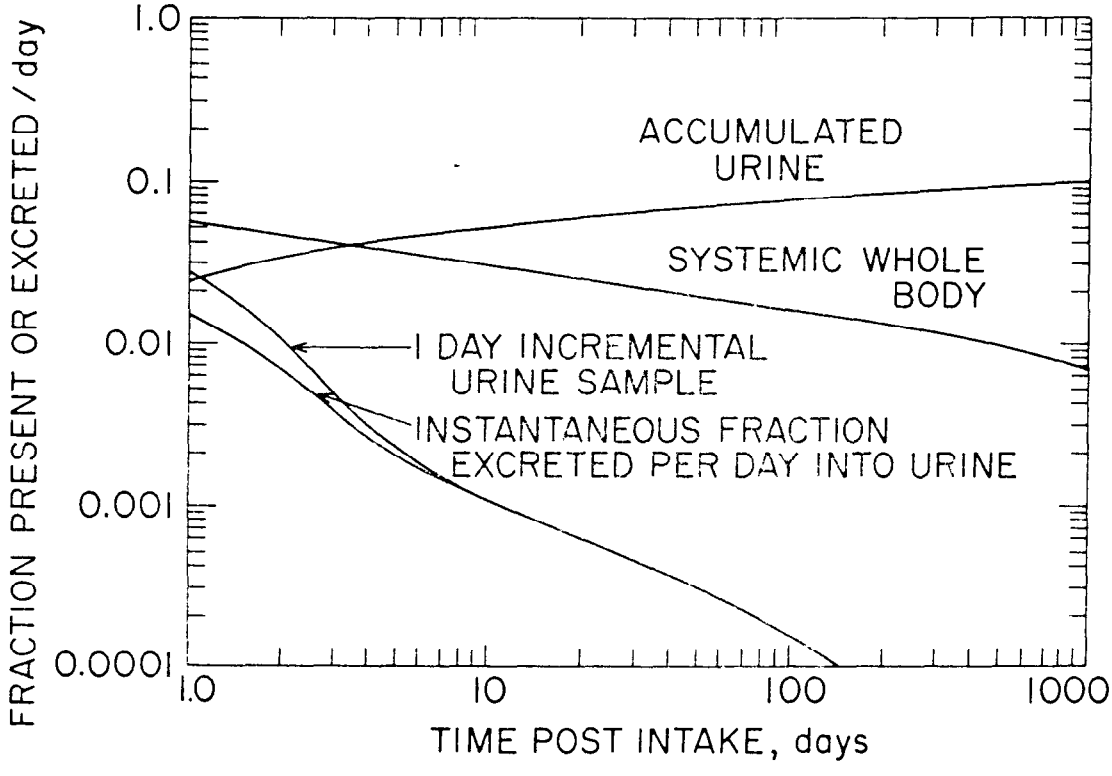

FIGURE 2.4 Systemic retention and urinary excretion post single inhalation intake of 1 micron AMAD aerosols of stable Class W cobalt for which $f_1 = 0.05$ and $f_u = 0.8$.

The straightness of these excretion curves are fortuitous. In fact, these curves embody: (1) the translocation of cobalt in and absorption of cobalt from compartments within the respiratory and GI tracts; (2) the delay in uptake of cobalt from these compartments; (3) the metabolism of cobalt within the systemic whole body including the recirculation of cobalt between cells and extracellular fluid; and (4) the final excretion of cobalt from the body, partially within urine.

To make an initial assessment of the significance of bioassay results, we recommend the use of intake retention functions that are based upon the ICRP or other appropriate Reference Man metabolic models. If the metabolic models are based upon the ICRP Publication 30 models, then the assessment will be consistent with annual limit on intake and derived air concentration quantities. In serious exposures, appropriate follow-up bioassay procedures should be used, along with information on the physical and chemical forms of radionuclides, in order to make a better estimate of the intake and dose and in order to provide guidance on possible medical procedures that might be used to reduce the committed dose. It would be difficult, in the usual case, to obtain values of all parameters for each exposed person. For practicality and other reasons, Reference Man metabolic models are best suited to the assessment of the significance of the bioassay data of workers in terms of estimated intakes. However, if suitable parameter values can be obtained for a specific individual, then they should be used to interpret the bioassay measurements, and these parameter values should be introduced to the available literature on radiation protection.